Attempted Hydrolysis of Ethyl Citrylideneacetate.—A mixture of 20 g. (0.09 mole) of ethyl citrylideneacetate, 48 cc. of water, and 6.4 cc. of sulfuric acid was vigorously refluxed for twenty hours. The ester layer became quite darkly colored during this period. The reaction mixture was poured into 200 cc. of water and extracted with 200 cc. of ether used in small portions. The dark red-brown ether solution was then extracted with four 25-cc. portions of 5% aqueous sodium hydroxide. These extracts were combined and acidified with phosphoric acid to yield a crude acid product, which was taken up in ether and dried over sodium sulfate. Distillation of the acid reaction product gave 1.8 g. of a light yellow oil, b. p. 142–151° (1 mm.), n^{25}D 1.5038. This produc twas not investigated further. Distillation of the neutral fraction gave 13.7 g. (68.5%) of unchanged ethyl citrylideneacetate, b. p. 135–150° (3.5 mm.), n^{25}D 1.5002, absorption maximum 277 mμ, ϵ 12,310.

A mixture of 20 g. (0.09 mole) of ethyl citrylideneacetate, 40 g. of water, 40 g. of glacial acetic acid and 20 g. of sulfuric acid was heated to reflux for five hours. The dark reaction mixture was diluted with 200 cc. of water and worked up as described above. Distillation of the acid reaction product gave 3.0 g. (17.2%) of a light yellow oil, b. p. 140–150° (2 mm.), n^{25}D 1.5091. This products howed an absorption maximum at 277 mμ, ϵ 3,100. Examination of the complete absorption curve (Fig. 2) indicates that this product consists principally of α-cyclocitrylideneacetic acid. Calcd.: neut. equiv., 194. Found: neut. equiv., 210 (92.3% acid purity). Distillation of the neutral reaction product gave 7.7 g. (38.5%) of a light yellow ester, b. p. 127–145° (5 mm.), n^{25}D 1.4952. This ester showed an absorption maximum at 282 mμ, ϵ 2,250. Examination of the complete absorption curve (Fig. 2) indicates that the product consists principally of ethyl α-cyclocitrylideneacetate. Calcd.: sapn. equiv., 222. Found: sapn. equiv., 209.

Cyclization of Ethyl Citrylideneacetate.—A mixture of 10 g. of concentrated sulfuric acid and 90 g. of 85% phosphoric acid was cooled to 3–4° in an ice-bath and mechanically stirred while 20 g. (0.09 mole) of ethyl citrylideneacetate was added dropwise during fifteen minutes. The cooling bath was then removed, and stirring was continued while the temperature rose to 25° during thirty minutes. The dark reddish brown reaction mixture was poured into 500 cc. of water, and the yellow, oily reaction product was taken up in ether, washed with water, and dried over sodium sulfate. Removal of the drying agent and ether followed by distillation under reduced pressure gave 10.1 g. (50%) of ethyl cyclocitrylideneacetate, b. p. 106–126° 0.4 mμ, n^{25}D 1.4879. Hydrolysis of this ester with alcoholic potassium hydroxide according to the procedure described above gave 5.8 g. (66% of the theoretical from the cyclized ester) of cyclocitrylideneacetic acid, b. p. 136–140° 0.4 mμ, n^{25}D 1.5070. The absorption curve for this product (Fig. 2) indicates that it is α-cyclocitrylideneacetic acid containing practically none of the open-chain or β-cyclic isomers. Calcd.: neut. equiv., 194. Found: neut. equiv., 225 (86.4% acid purity).

Ethyl citrylideneacetate, 15 g. (0.068 mole), was stirred at room temperature with a solution of 6.0 g. of concentrated sulfuric acid in 60 g. of glacial acetic acid. On working up this mixture as described above, 8.6 g. (57.4%) of ethyl citrylideneacetate was recovered, unchanged as evidenced by its refractive index and absorption curve, n^{25}D 1.5015, absorption maximum, 277 mμ, ϵ 11,000.

A number of similar experiments were performed in an attempt to cyclize ethyl citrylideneacetate and the free acid using such strongly acidic reagents as 100% phosphoric acid and high concentrations of sulfuric acid (50% and greater) in water, acetic acid and 85% phosphoric acid. All such attempts led to undistillable tars.

Absorption Spectrum Measurements.—Determinations of ultraviolet spectra were made on the Beckman Spectrophotometer, Model DU. The solvent was 95% ethanol.

Summary

1. The Reformatsky reaction has been applied to the synthesis of ethyl citrylideneacetate, and this ester has been hydrolyzed to citrylideneacetic acid.

2. Pure α- and β-cyclocitrylideneacetic acids have been prepared by hypochlorite oxidation of the corresponding ionones.

3. The ultraviolet absorption spectra of these compounds have been determined.

4. A study has been made of the cyclization of ethyl citrylideneacetate by various acidic reagents. Most satisfactory results were obtained using small concentrations of sulfuric acid in sirupy phosphoric acid as cyclizing agent; this procedure yielded a product consisting principally of ethyl α-cyclocitrylideneacetate. No conditions of cyclization were found which would yield the β-cyclo ester as the major product.

ATLANTA, GEORGIA RECEIVED JULY 29, 1946

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, THE UPJOHN COMPANY]

An Improved Synthesis of β-Alanine. III. The Addition of Ammonia to Acrylonitrile at 50–150°[1]

BY JARED H. FORD, SAUL R. BUC[2] AND J. WARD GREINER

In a previous paper from these Laboratories[3] it was shown that the reaction of ammonia with acrylonitrile gave higher yields of β-aminopropionitrile with aqueous than with liquid ammonia.[4,5] Although it was demonstrated that higher temperatures favored the formation of the primary amine our previous studies were restricted to the temperatures spontaneously attained in closed vessels after mixing the reactants at room temperature. Since this gave the undesired secondary amine, di-(β-cyanoethyl)-amine, as the major product of the reaction, it seemed advisable to extend the studies to include higher temperatures.

Experimental

Preliminary experiments at moderate pressures (less than 75 p. s. i.) were made in a 36-inch length of 3-inch Pyrex pipe, the top of which was closed by a rubber stopper that was held in place by a steel plate bolted to

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[1] Part II, Ford, THIS JOURNAL, **67**, 876 (1945).

[2] Present address: General Aniline and Film Corporation, Easton, Pennsylvania.

[3] Buc, Ford and Wise, THIS JOURNAL, **67**, 92 (1945).

[4] Hoffmann and Jacobi, U. S. Patent 1,992,615.

[5] Whitmore, Mosher, Adams, Taylor, Chapin, Weisel and Yanko, THIS JOURNAL, **66**, 725 (1944).

the flange supplied with the pipe. The reservoir for the acrylonitrile, a piece of 3-inch iron pipe capped at both ends and provided at the top with a plug for filling, a pressure gage and a petcock for the release of pressure, was connected to the reaction vessel by two pieces of $^1/_8$ inch iron pipe, one of which served as a pressure equalizer while the bottom outlet, a section of which was replaced with cloth reinforced rubber tubing so that the flow could be regulated with a screw clamp, joined a glass tube extending to bottom of the Pyrex pipe in which a thermometer was suspended from the rubber stopper.

In operation the 28% aqueous ammonia was placed in the Pyrex pipe and heated to the desired temperature by means of a water-bath. Rapid introduction of (about three minutes were required to drain the reservoir) the lighter acrylonitrile at the bottom of the reaction tube assured adequate mixing. The temperature of the solution dropped slightly at first and then rose about 30°. When the reaction mixture had cooled to room temperature the water and ammonia were distilled off rapidly at 30–40 mm. pressure and the residual liquid was distilled from an ordinary Claisen flask at 5–8 mm. pressure. The crude β-aminopropionitrile fraction collected at 60 to 110° was found to give 92–95% of pure β-aminopropionitrile, b. p. 70–72° (10 mm.), upon redistillation through a 30-cm. packed column.

Under these conditions the results were similar to those obtained previously,[3] *i. e.*, the yield of β-aminopropionitrile increased with rise in temperature. Using four moles of ammonia per mole of acrylonitrile the yields were 42 and 51% at 50 and 70°, respectively, with maximum pressures of 40 and 75 p. s. i.

These results indicated that still higher temperatures should be studied. For this examination two Aminco high pressure hydrogenation bombs having capacities of 300 and 3800 ml. were used. The smaller one was charged with 200–250 ml. of acrylonitrile, filled with hydrogen to a pressure of 1200–1500 p. s. i., and attached in an inverted position to the larger bomb which contained the aqueous ammonia. When the ammonia had been heated to the desired temperature the valve was opened and the acrylonitrile was blown into the larger bomb. With introduction of the acrylonitrile above the surface of the ammonia, the yield of β-aminopropionitrile did not increase with temperature as rapidly as anticipated from preliminary work. Apparently some of the reaction took place above the surface where the ratio of ammonia to acrylonitrile was low for the yields improved when the nitrile was introduced below the surface. This was accomplished by tapping a steel tube into the cap of the larger bomb so that it extended very close to the bottom.

At temperatures above 100° the yields decreased with increasing temperatures and the residues from the distillation of the primary amine were more viscous. A marked improvement was noted when the reaction time was shortened. Since it was not feasible to cool the large bomb quickly, about one minute after the acrylonitrile had been added the smaller bomb was disconnected and replaced by a short length of rubber tubing which was connected to the top of a water cooled coil condenser. When the valve was opened the internal pressure of the larger bomb forced the contents out through the condenser where they were collected in a flask that was equipped with a tube leading to the hood. Vaporization of the ammonia greatly facilitated the cooling. By this method the contents of the bomb could be vented in about two minutes and were at the high temperature only about five minutes.

The residues from distillation of the primary amine were not examined further since they had previously been found to consist largely of secondary amine[3] and small amounts of tertiary amine.[6] In studying the over-all material balance the residues were weighed and assumed to be secondary amine. This accounted for only 80–94% of the acrylonitrile and the discrepancies increased with the excess of aqueous ammonia employed, indicating that β-aminopropionitrile was being lost during concentration of the reaction mixtures.

In concentrating a 20% aqueous solution of pure β-aminopropionitrile under the conditions that were used for working up reaction mixtures, 81% of the nitrile was recovered by distillation of the residue and 18% was present in the aqueous distillate (determined by titration). When a similar solution was distilled through an 18-inch packed column at a 3:1 reflux ratio the distillate contained only traces of nitrile, indicating that the losses were due to poor fractionation rather than the formation of an azeotropic mixture.

A precise fractional distillation of the reaction mixtures did not appear to be feasible because of the time involved but by assuming the distillation residues to be secondary amine the yield of primary amine was estimated by subtracting the equivalents of secondary amine from the moles of acrylonitrile that were used in the reaction. In order to check the accuracy of this method of estimating yields a mixture containing 0.70 mole of β-aminopropionitrile, 0.15 mole di-(β-cyanoethyl)-amine and 4 moles of 28% ammonia was prepared and worked up under the same conditions that were used for the reaction mixtures. The recovery from this synthetic mixture was almost exactly the same as that from an actual reaction mixture (see line 11 of Table I) which gave an estimated yield of 70%, *i. e.*, the yield of primary amine was 58% and the residue, assuming it to be secondary amine, was 30%.

TABLE I

YIELDS OBTAINED BY REACTION OF 28% AQUEOUS AMMONIA WITH ACRYLONITRILE

Starting temp. of ammonia, °C.	Maximum pressure[i]	Per cent. yield of R[j]NH$_2$ obs.[k]	R$_2$NH estd.	Total recovery[l]	Estimated yield of RNH$_2$
55[a,d]	34	41	49	90	51
94[a,d]	103	46	45	91	55
113[a,d]	157	47	45	92	55
135[a,d]	190	43	47	90	53
45[b,d]	50	38	54	92	46
74[b,d]	115	51	39	90	61
99[b,d]	140	55	38	93	62
130[b,d]	175	49	41	90	59
150[b,d]	>300	36	57	93	43
90[c,d]	140	53	34	87	66
110[c,d]	215	59	30	89	70
133[c,d]	>300	57	31	88	69
200[c,d]	700	42	48	90	52
96[c,e]	120	23	68	91	32
98[c,f]	160	44	46	90	54
103[c,g]	140	51	37	88	63
90[c,h]	230	61	22	83	78
112[c,h]	290	65	18	83	82

[a] Acrylonitrile added above the surface; not vented (*i. e.*, cooled slowly in reaction vessel). [b] Acrylonitrile added below the surface, not vented. [c] Acrylonitrile added below the surface; vented (*i. e.*, cooled rapidly by discharging from reaction vessel). [d] Four moles of ammonia per mole of acrylonitrile. [e] One mole of ammonia per mole of acrylonitrile. [f] Two moles of ammonia per mole of acrylonitrile. [g] Three moles of ammonia per mole of acrylonitrile. [h] Ten moles of ammonia per mole of acrylonitrile. [i] Pounds per square inch (gage). Includes hydrogen. [j] R = —CH$_2$CH$_2$CN. [k] Crude product; b. p. 60–110° at 5–8 mm. [l] Per cent. acrylonitrile accounted for as primary amine or residue.

Discussion of Results

Rapid addition of acrylonitrile below the surface of an excess of aqueous ammonia, preheated to about 110° and used most practically in a three

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(6) Wiedeman and Montgomery, THIS JOURNAL, **67**, 1994 (1945).

or four to one mole ratio, with a reaction period of two to five minutes followed by rapid cooling of the products to prevent secondary reactions gave 55–60% yields of β-aminopropionitrile with an additional 10% lost in the aqueous distillates. Adding the nitrile above the surface or allowing the reaction mixtures to remain hot for extended periods of time caused serious losses in the yield (see Fig. 1). The use of a large excess of ammonia increased the yield (see Fig. 2) of primary amine (*e. g.*, with a 10:1 mole ratio the yield was 80%) in the reaction mixture but it was attended by a corresponding increase in distillation losses.

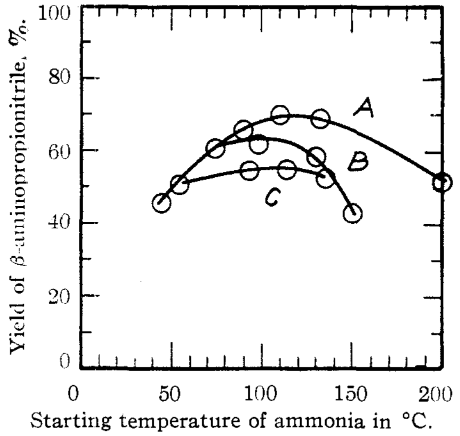

Fig. 1.—Effect of temperature on yield of β-aminopropionitrile using 4 moles of ammonia per mole of acrylonitrile: A, nitrile added below surface, vented; B, nitrile added below surface, not vented; C, nitrile added above surface, not vented.

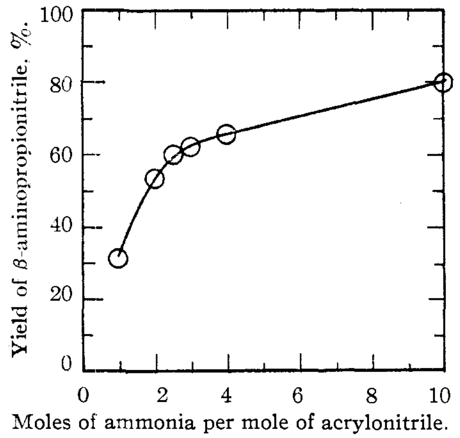

Fig. 2.—Effect of mole ratio on yield of β-aminopropionitrile at 95–105°.

McElvain and Stork[7] have shown that in the reaction of ethyl acrylate with ammonia the following equilibrium ($R = COOC_2H_5$) exists at room temperature

$$\begin{tikzcd} N(CH_2CH_2R)_3 \arrow[r, shift left] & NH(CH_2CH_2R)_2 + CH_2{=}CHR \arrow[l, shift left] \arrow[d, shift left] \\ NH_3 + CH_2{=}CHR \arrow[r, shift left] & NH_2CH_2CH_2R + CH_2{=}CHR \arrow[l, shift left] \arrow[u, shift left] \end{tikzcd}$$

They isolated 42% of the tertiary amine, 44% of the secondary amine, "practically none" of the primary amine and noted the presence of unreacted ethyl acrylate. In the present investigation ($R = CN$) no unreacted acrylonitrile has been detected in the reaction mixtures and the principal products are the primary and secondary amines. The indications are that the above equilibrium is not the principal factor which determines the yield of primary amine. The fact that the yields depend upon the manner in which the acrylonitrile is added to the ammonia (below or above the surface) makes it seem probable that under our experimental conditions the yields are determined largely by the relative rates of the following reactions

$$CH_2{=}CHCN + NH_3 \longrightarrow NH_2CH_2CH_2CN \tag{1}$$

$$CH_2{=}CHCN + NH_2CH_2CH_2CN \longrightarrow NH(CH_2CH_2CN)_2 \tag{2}$$

and that the reaction time is not long enough for the equilibrium between primary and secondary amines to become established. The fact that an equilibrium between the primary and secondary amines can exist was demonstrated by adding pure secondary amine to two moles of aqueous ammonia at 156° for ten minutes and isolating twenty per cent. of primary amine from the mixture. No attempt was made to find the composition of the true equilibrium mixture. This determination would be complicated by the fact that the rate of hydrolysis of the nitriles becomes appreciable at temperatures as low as 150°.[8]

Summary

1. The reaction of acrylonitrile with aqueous ammonia has been studied over the temperature range of 50 to 150°.

2. The highest yields of β-aminopropionitrile (60–80%) were obtained when the ammonia was preheated to about 110°, the acrylonitrile was added rapidly below the surface and the mixture was allowed to react for two to five minutes.

KALAMAZOO, MICHIGAN RECEIVED OCTOBER 19, 1946

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[7] McElvain and Stork, THIS JOURNAL, **68**, 1049 (1946).

[8] Carlson and Hotchkiss, U. S. Patent 2,335,997; Carlson, U. S. Patent 2,336,067.